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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/629,261	DONG, ZHENG XIN	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 19* is/are pending in the application.

4a) Of the above claim(s) *6,9 and 12-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,8,10,11 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to preliminary amendment (filed 8/25/05), claim 19 has been added. Claims 1-16 & 19 are now pending

Applicants' election of Group I is acknowledged, as is the elected specie (the peptide of SEQ ID NO: 55), to which claim 19 is solely directed.

Claims 1-5, 7, 8, 10, 11, 19 are examined in this Office action; claims 6, 9, 12-16 are withdrawn from consideration.

✦

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,903,186.

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of copending application Serial No. 11/145782. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

✦

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 8, 10, 11, 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

On pages 14-15, a procedure is given for assessing the propensity of a compound to displace (^{125}I) GLP-1(7-36) from RIN 5F rat insulinoma cells expressing the GLP-1 receptor. However, no result was given for this assay, and so there is no basis for concluding that the peptide of SEQ ID NO: 2 exhibits any capacity to bind to the GLP-1 receptor. It may well be the case that other analogs of GLP-1 bind to the GLP-1 receptor, but structure/activity relationships are unpredictable; i.e., one cannot predict GLP receptor binding merely by viewing the structure of a compound. Accordingly, "undue experimentation" would be required to use the compound of claim 10 to displace (^{125}I) GLP-1(7-36) from RIN 5F rat insulinoma cells expressing the GLP-1 receptor.

✦

Claims 1-5, 7, 8, 10, 11, 19 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 1, variable A^{12} can be X^1-Phe. However, the meaning of "X^1-Phe" is unclear. Is it the case that X^1 must be bonded to the aryl group of the phenylalanine, or can X^1 be bonded to the *alpha*-amino group?

- In claim 1, reference is made to the denotation "N_M", for example, the following:

  $Lys^{26,34}$-bis(N_M-alkanoyl))hGLP-1

  However, it does not appear that the term "N_M" is defined. Perhaps the "M" is intended to convey the greek letter *epsilon*, but whatever the case, the meaning of "N_M" is not made clear.

- In claim 1, part (vi) a genus of compounds is excluded. It is recited that the compound is not Z^1-hGLP-1(7-36, 7-37 or 7-38)-OH.
  Normally, when a substituent variable is placed adjacent to the N-terminus of a peptide, with a hyphen between the two, the formula thus obtained signifies that the substituent variable in question is bonded to the N-terminus of the peptide. Thus, applicants' denotation could be interpreted to mean that what is excluded is compounds in which "Z^1" is bonded to the N-terminus of the hGLP-1(7-36, 7-37 or 7-38)-OH.
  If so, it is unclear which compounds are to be excluded.

  A related issue concerns part (vii) of the exclusions. It is recited that the compound is not a combination of any two of the substitutions listed in vi(a) to vi(d). Consider the first three compounds which applicants are attempting to refer to in part (a) of part (vi). They are the following: Arg^{26}, Arg^{34}, and $Arg^{26,34}$. What compound exactly do applicants believe is obtained by combining $Arg^{26,34}$ Glp-1(7-36) with Arg^{26} Glp-1(7-36) ....? Similarly, which compound do applicants believe is obtained by combining Arg^{34} Glp-1(7-36) with $Arg^{26,34}$ Glp-1(7-36)...?

- In claim 4, A^{22} is defined as one of 3 amino acids, the first of which is glycine, and the third of which is amino-isobutyric acid. What is the second amino acid of the three?

- Claim 1 mandates that R^2 and R^3 both be hydrogen. In addition, there are several subgenera that are excluded from the scope of the claimed genus; these are listed in the last 25 (or so) lines of claim 1. In the

sixth line from last (of claim 1), there is a proviso that excludes the N-terminal histidine from being alkylated or acylated. However, claim 1 does not otherwise permit such a substitution anyway. Accordingly, the proviso (sixth line from last) is superfluous.

✦

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 are rejected under 35 U.S.C. §102 (b) as being anticipated by Buckley (USP 5,545,618).

Buckley provides (col 2, line 56+) the sequence of native GLP-1(7-37), which is the following:

HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

Buckley also discloses GLP-1(7-34) and GLP-1(7-35). Claim 1, however, does not clearly exclude these. For example, in the case of GLP-1(7-35), there is one amino acid difference between this and the native GLP-1(7-36). That amino acid would be the arginine at position 36. Thus, one could say that there is one amino acid difference between GLP-1(7-35) and GLP-1(7-36)

Thus, the claims are anticipated.

✦

The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Buckley (USP 5,545,618).

Buckley provides (col 2, line 56+) the sequence of native GLP-1(7-37), which is the following:

HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

This particular peptide is excluded by the claims. The issue raised in this ground of rejection is that there are several amino acid substitutions which are rendered obvious by the disclosure of this sequence. For example, a peptide which contains glutamic acid at a given position is obvious over an otherwise identical peptide which bears an aspartic acid at the same position. Glutamic acid and aspartic acid, of course, differ by just one methylene unit in the side chain. A peptide biochemist of ordinary skill would have expected, *a priori*, that when a side chain of one amino acid in a peptide is extended by one methylene unit, the biological activity of that peptide will remain substantially the same. The court recognized this to be the case in *In re Shetty* (**195** USPQ 753) and *In re Hass & Susie* (**60** USPQ 544). Similarly, by extending the methyl group of (the side chain of) valine by one methylene unit, one obtains isoleucine. By extending the side chain of arginine by one methylene unit, the result is homoarginine. Thus, for example, each of the following is rendered obvious by the disclosure of native GLP-1(7-37):

HA**D**GTFTSDVSSYLEGQAAKEFIAWLVKGRG

HAEGTFTS**E**VSSYLEGQAAKEFIAWLVKGRG

HAEGTFTSD**I**SSYLEGQAAKEFIAWLVKGRG

HAEGTFTSDVSSYLEGNAAK**D**FIAWLVKGRG

HAEGTFTSDVSSYLEGQAAKEFVAWLVKGRG

HAEGTFTSDVSSYLEGQAAKEFIAWLIKGRG

HAEGTFTSDVSSYLEGQAAKEFIAWLVXGRG (X = ornithine)

HAEGTFTSDVSSYLEGQAAKEFIAWLVKGXG (X = homoarginine)

Thus, the claims are rendered obvious.

✧

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Kjeldsen (USP 6,214,547).

Kjeldsen discloses (col 9, line 36) GLP-1(7-39). Kjeldsen does not provide the sequence of GLP-1(7-39), but this is known in the art. In particular, a glycine resides at position 37, and an arginine is present at positions 38 and 39.

Thus, the claim is rendered obvious.

✧

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Knudsen (WO 98/08871)

Knudsen discloses various GLP-1 analogs, for example, those listed on pages 19-30. Applicants have attempted to exclude many of these, but without success. The first point is that, as indicated above in the §112, 2nd paragraph rejection, the term "N_M" is not defined. This rejection could stop there and be sufficient. It may turn out, at some point in the future, that applicants intend for "M" to

convey the greek letter *epsilon*. Should that event come to pass, this ground of rejection will still be maintained. First, while it may be that applicants intend to exclude some GLP-1 derivatives in which a lysine amino group is acylated with an alkanoic acid, Knudsen discloses various GLP-1 analogs in which the lysine is acylated with something other than an alkanoic acid. For example, there are several examples of lysines acylated with a carboxynonadecanoyl group; there are also examples of lysines acylated with a deoxycholic acid group. These are not excluded.

There is also another point to be made, which is that the exclusions, to the extent that they exist, only apply for the case of "E" representing OH or NH_2. The exclusions do not apply for the case of "E", taken together with the carbonyl group to which it is bonded, representing a carboxylate salt. As applicants may be aware, it is quite common for pharmaceutical chemists to prepare the salts of compounds prior to administration. Applicants may have excluded some compounds which bear a (protonated) carboxyl group at the C-terminus, but applicants have not excluded any carboxylate salts.

Thus, for several reasons, the claim is rendered obvious.

Reference "AE" was stricken from the IDS because a translation has not been provided. In fact, even an abstract has not been provided. What has been provided (that is in English) is a list of patent family members.

The remaining references that were stricken from the IDS were so treated because they were not received.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at (571)272-0974. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800